Dr. Irena Kopwowska 334 Fairhill Road Wynnewood, Pennsylvania

Dear Irena:

Thank you for your letter of April 17, and for sending me the copy of your application.

I am very glad to see that you have reacted so vigorously to the suggestion on the cytohormonal stady. I am a little concerned that the NIH may find this too ambitious a project to jump into without any preparatory stady at all, but perhaps the most pessimistic outlook would be that they might cut back on your application during its early development to give some chance to see how things worked. This should not seriously prejudice the success of what you want to do, and I hope you will not be personally discouraged by any such actions if this is what happens.

As to the technical content of the proposal, my principle reaction which is, of course, based also on a large measure of personal confidence is that it is very good. It might have been better to concentrate much more on the main point, the retrospective study, to give adequate emphasis to the need for the collection of a very large sample and so forth. The other issues are in many respects more interesting, but also more speculative and necessarily have to be stated more vaguely, and to some extent they may weaken the impact of the application. This would apply particularly to the long term yield from your project three, page seven (but I certainly agree with you that these studies are urgently required).

The main thing I have to criticize - see also page seven, paragraph two - there is some implication that we have some good idea as to therapeutic management of chromosomal abnormality syndromes. Unfortunately, so far as I know, this is just not the case. However, it is hard to see just how we can ever develop the necessary information for the management of mental deficiency without the means to make just such studies on the very early development of these aneuploid children.

I hope to be hearing more from you. Lots of luck,

Yours sincerely.

Joshua Lederberg Professor of Genetics